

Claims

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1. A forecasting method of the pharmacokinetics of a lipid A analog in an injection preparation containing the lipid A analog or a pharmacologically acceptable salt thereof, which comprises measuring at least one of membrane fluidity and circular dichroism thereof. *to forecast...?*

2. The forecasting method according to claim 1, which is conducted *for what?* for evaluating the injection preparation.

3. The forecasting method according to claim 1, which ^{is} conducted for quality evaluation in order to obtain an injection preparation exhibiting constant pharmacokinetics.

4. The forecasting method according to claim 1, which is conducted in the preparation step of the injection preparation. ?

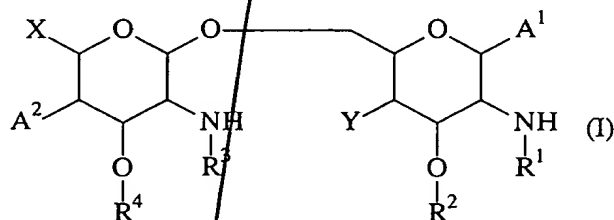
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5. The forecasting method according to claim 1, wherein the membrane fluidity is measured by fluorescence probe method which uses, as parameters, at least one of order parameter (S), fluorescence polarity (P) and fluorescence anisotropy (r).

6. The forecasting method according to claim 1, wherein the injection, which contains aggregates having a diameter not greater than 30 nm, ^{is} prepared by dissolving the lipid A analog or a pharmacologically acceptable salt

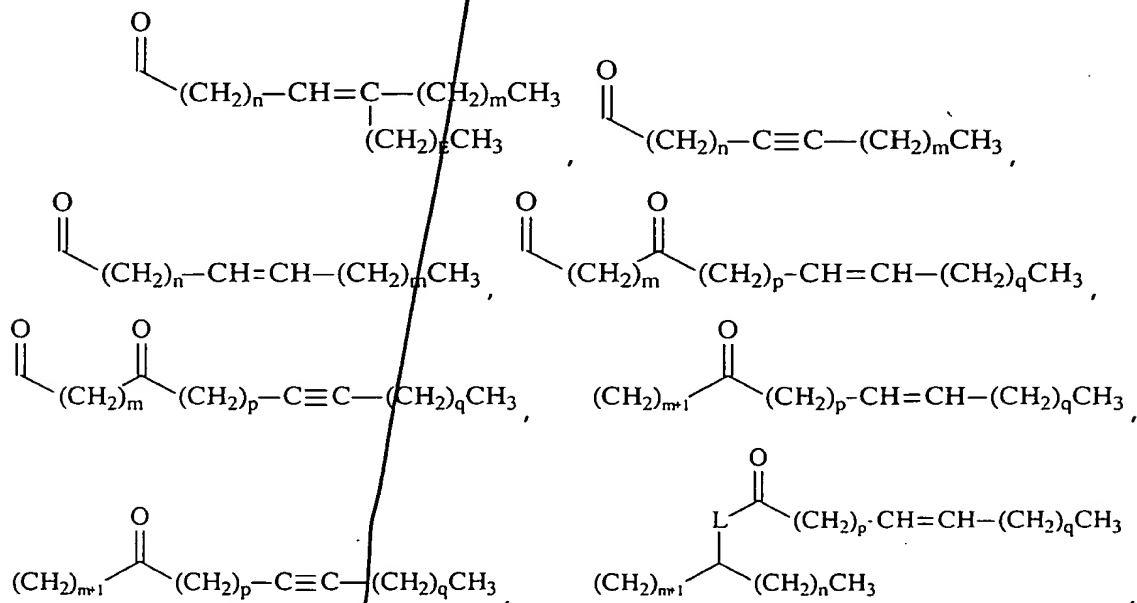
thereof in an alkaline aqueous solution and then adding a buffer thereto.

7. The forecasting method according to claim 1, wherein the injection preparation is an aqueous injection or freeze-dried preparation.

8. The forecasting method according to claim 1, wherein the lipid A analog or a pharmacologically acceptable salt thereof is a compound represented by the following formula (I):

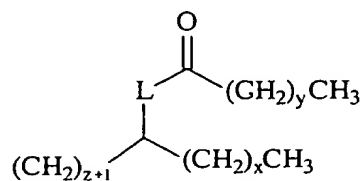
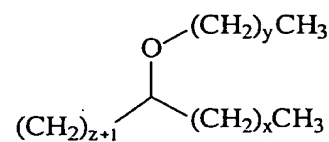
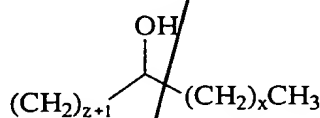
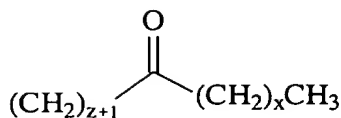
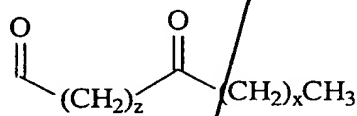
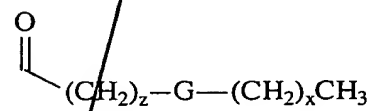
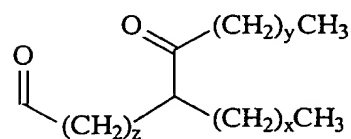
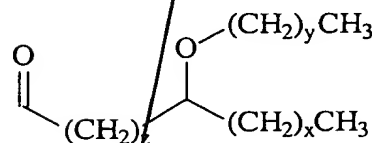
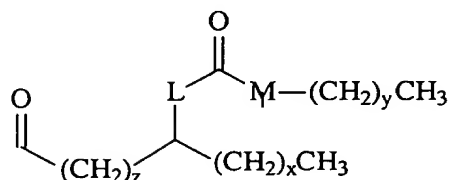
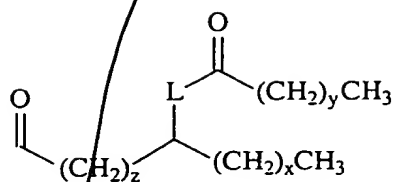
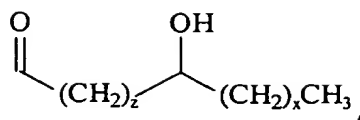
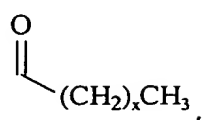


wherein at least one of R^1 , R^2 , R^3 and R^4 is

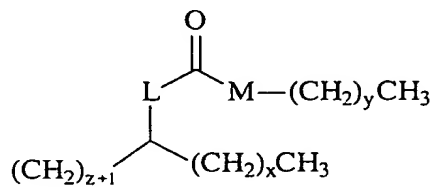




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or



wherein each L is O, N or C; each M is O or N; each x independently is an integer of 0 to 14; each y independently is an integer of 0 to 14; each z independently is an integer of 0 to 10; each G independently is N, O, S, SO or SO₂.

A¹ and A² are, independently of one another, H, OH, OCH₃,

wherein each d independently is an integer of 0 to 5; each
f independently is an integer of 0 to 5; each g
independently is an integer of 0 to 5; each A³
independently is

$$\begin{array}{ccccc}
 \text{(CH}_2\text{)}_j\text{—O—P(=O)(OH)}_2 & & \text{O—(CH}_2\text{)}_{j+1}\text{—O—P(=O)(OH)}_2 & & \text{(CH}_2\text{)}_j\text{—P(=O)(OH)}_2 \\
 & & & & \\
 \text{O—(CH}_2\text{)}_j\text{—P(=O)(OH)}_2 & & \text{(CH}_2\text{)}_j\text{—CO}_2\text{H} & \text{or} & \text{O—(CH}_2\text{)}_j\text{—CO}_2\text{H}
 \end{array}$$

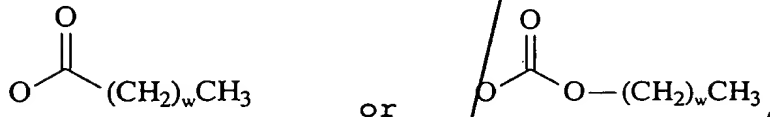
wherein each j independently is an integer of 0 to 14,
X is H, $(\text{CH}_2)_t\text{CH}_3$, $(\text{CH}_2)_t\text{OH}$, $(\text{CH}_2)_t\text{O}(\text{CH}_2)_v\text{CH}_3$, $(\text{CH}_2)_t\text{OPO}(\text{OH})_2$,
 $(\text{CH}_2)_t-\text{CH}=\text{CH}-(\text{CH}_2)_v\text{CH}_3$, $(\text{CH}_2)_t-\text{O}-\text{R}^5$,

$$\begin{array}{c} \text{HC} \begin{array}{l} \diagup \text{O} - (\text{CH}_2)_t \text{CH}_3 \\ \diagdown \text{O} - (\text{CH}_2)_v \text{CH}_3 \end{array} \end{array} \quad \text{or} \quad \left[\begin{array}{c} \text{H}_2 \\ | \\ \text{OH} \end{array} \right]_t - \text{CH}_3$$

wherein t and v , are independently of one another, an

integer of 0 to 14; R^5 is any of the above definitions of R^1 to R^4 ,

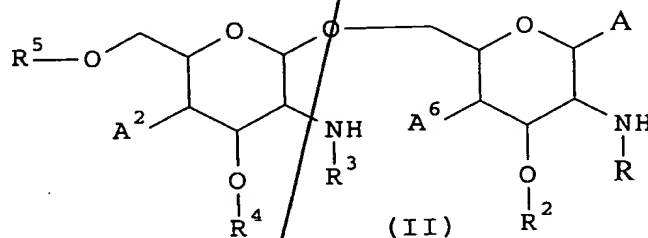
Y is H, OH, $O(CH_2)_wCH_3$, a halogen atom,



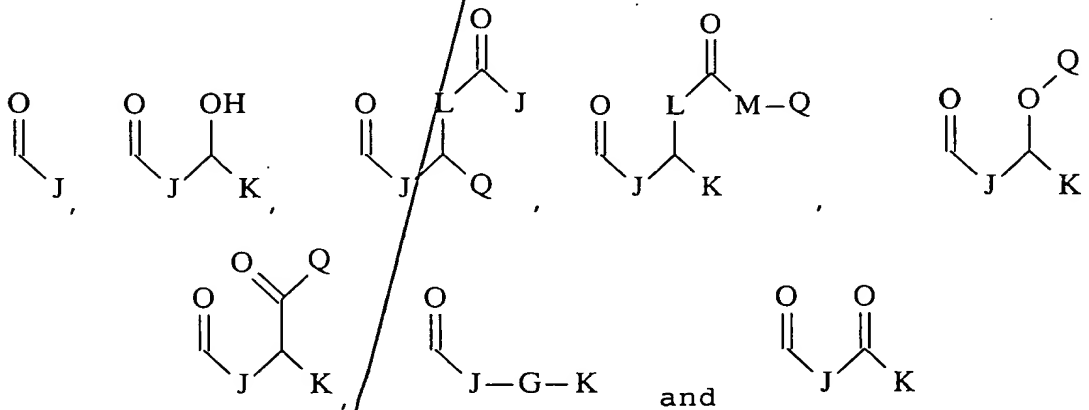
wherein w is an integer of 0 to 14,

or a pharmacologically acceptable salt thereof.

9. The forecasting method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (II):

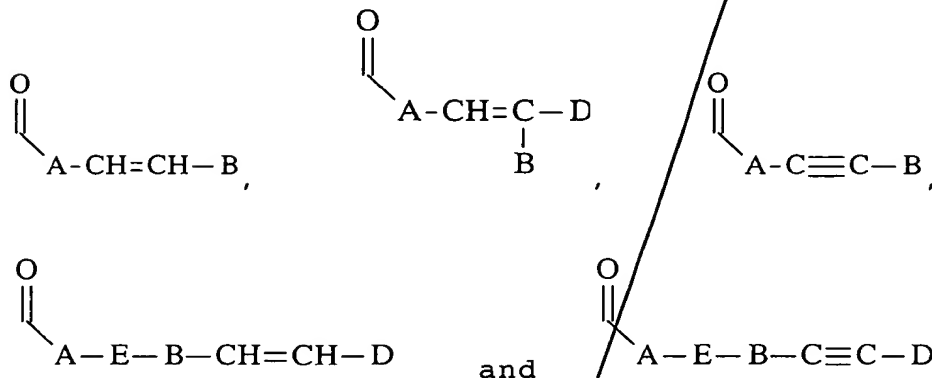


wherein R^1 is a group selected from the groups consisting of

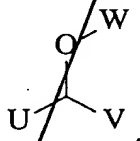


wherein J, K and Q are each a linear or branched alkyl group of 1 to 15 carbon atoms; L is O, NH_2 or CH_2 ; M is O or NH ; G is NH , O, S, SO or SO_2 ,

R^2 is a linear or branched alkyl group of 5 to 15 carbon atoms, R^3 is a group selected from the groups consisting of



wherein E is N, O, S, SO or SO₂; A, B and D are each a linear or branched alkyl group of 1 to 15 carbon atoms, R^4 is a group selected from the groups consisting of a linear or branched alkyl group of 4 to 20 carbon atoms and

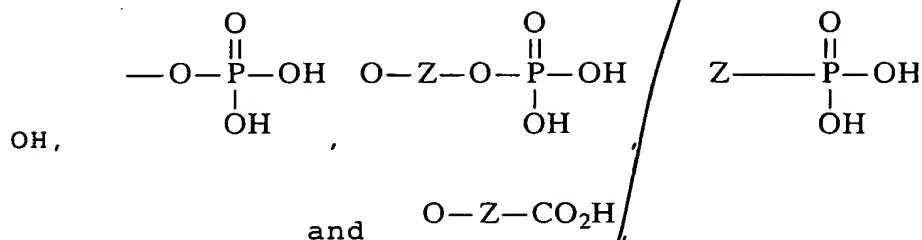


wherein U and V are each a linear or branched alkyl group of 2 to 15 carbon atoms; W is a hydrogen atom or a linear or branched alkyl group of 1 to 5 carbon atoms,

R^5 is a group selected from the groups consisting of a hydrogen atom, J' , $-J'-\text{OH}$, $-J'-\text{O}-K'$, $-J'-\text{O}-K'-\text{OH}$ and $-J'-\text{O}-\text{PO}(\text{OH})_2$, wherein J' and K' are each a linear or branched alkyl group of 1 to 5 carbon atoms,

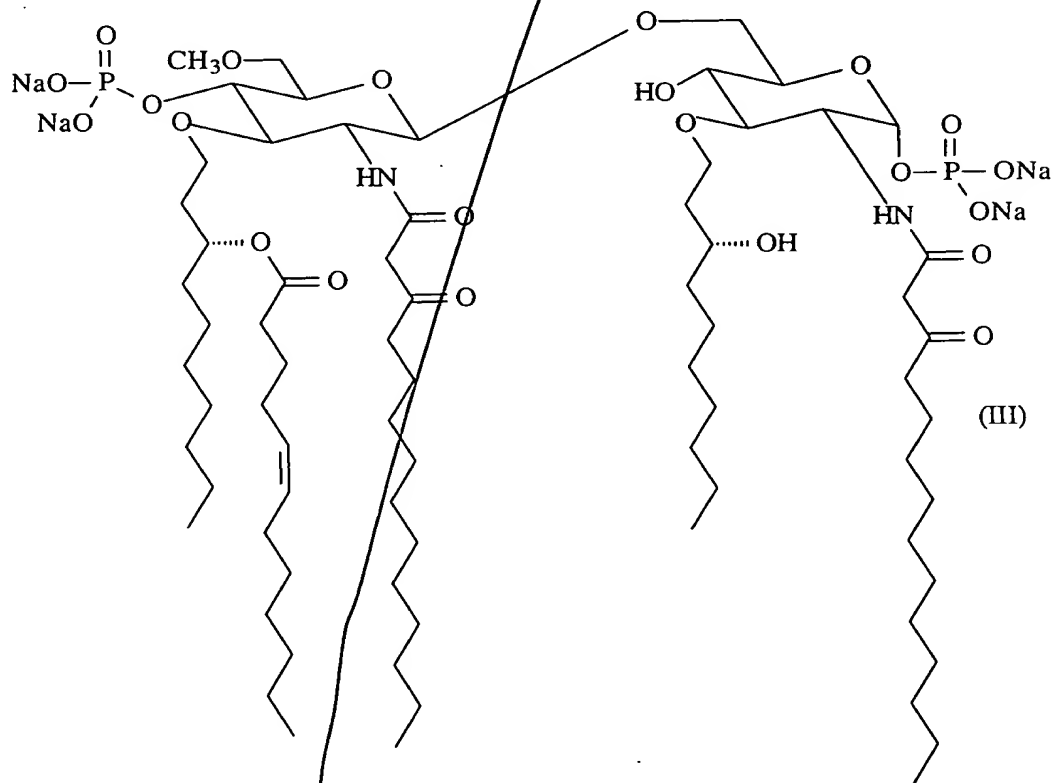
R^6 is a group selected from the groups consisting of a hydroxyl group, a halogen atom, an alkoxy group of 1 to 5 carbon atoms, and an acyloxy group of 1 to 5 carbon atoms.

A¹ and A² independently are each a group selected from the groups consisting of

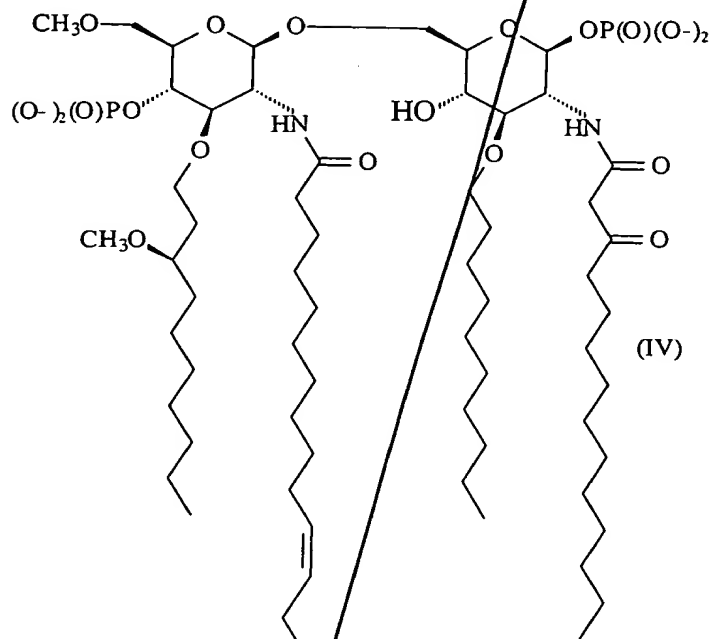


wherein Z is a linear or branched alkyl group of 1 to 10 carbon atoms, or a pharmacologically acceptable salt thereof.

10. The forecasting method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (III):



11. The forecasting method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (IV):



12. The forecasting method according to claim 1, wherein the lipid A analog or a pharmacologically acceptable salt thereof has an aggregate structure in the form of endoplasmic reticulum with lipid biomolecular membrane or micelle.